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MEDICAL CONTROL OF INDUSTRIAL EXPOSURE TO TOXIC CHEMICALS

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(Concluded from February issue)

EXTERNAL FACTORS.

Abnormal blood pressure scores may be produced by any conditions which interfere with the normal metabolic processes of tissues. Thus, they may result from:

- Improper nutrition (improper as to quantity, quality, timing, and especially vitamin content).
- Improper medication (unnecessary or badly controlled use of the "sulfa" drugs.
- Self-medication (the use of "pick-meups" containing drugs such as aniline derivatives: also alcohol).
- Unnecessary exposure to abnormal climatic conditions.
- Unnecessary exertion, leading to fatigue.
- 6. Disease (which is, in essence, chemical poisoning).
- Deprivation of oxygen (resulting from sudden transfer to great altitudes or prolonged work in ill-ventilated enclosures).
- 8. Any combination of one or more of the

These factors may act quite independently of the worker's occupation. They are, very decidedly, situations over which he should have control, or might control, if he were properly advised. They are extremely important in industrial maintenance of health.

NUTRITION

The state of nutrition of the nation is receiving intensive study since Selective Service medical examinations disclosed a high proportion of men of military age with defects obviously due to faulty metabolism. Daily, evidence grows that many people have

not received properly balanced diets. Claims that such is not the case are based chiefly on determinations of the vitamin content of raw There is practically no information on the vitamin content of foods as eaten; i. e., after kitchen manipulations have destroyed part or all of the important components. Our own work has shown conclusively that exposure to chemicals can interfere with the ordinary metabolism of vitamins and that those exposed to harmful substances in industry can be protected, to a considerable degree, against the early signs of action of such materials by a maximum daily intake, especially of vitamin C and the B group. It is interesting to note that clinical C and B deficiencies can produce almost the same group of symptoms as are found in early action of toxic industrial chemicals. lowered muscle tonus produced by chemicals may also be present in B, and C deficiencies.

In theory, dietary deficiencies among workers should be adjusted by proper education. Actually, an educational program has been carried on throughout this Nation for many years, and apparently without success as yet. In war production, time is important. However intense the program of education now set up, regional traditions and personal fancies will act against complete success.

It is important to realize that the diet of workers must be adequate not merely as to quantity and vitamin content, but also as to distribution through the day. The total daily intake may be ample, but if confined to one large meal it may leave a rather long period during which the stomach is relatively empty. During the first World War, it was noted that improper distribution of meals could be a source of great disability in workers exposed to TNT. Many plant surveys show that men coming off the early morning (12 to 8) shift show abnormal blood pressure scores more frequently than workers on other

shifts. This may be due partly to lack of adaptation to night work, but it also may be due to lack of proper distribution of food intake.

Control of the diet of workers is particularly difficult in war plants. The size and layout of many plants make it hopeless to expect men to go to a central cafeteria for lunch. It is difficult to assure both adequate food intake and cleanliness of eating conditions. In such circumstances it seems to us reasonable and proper to supplement the worker's diet by concentrated vitamin preparations, containing at least a daily dose of 1 mg. of B₁ and 100 mg. of vitamin C.

MEDICATION

Chemicals used in therapeutics may have the same early physiological action as those absorbed in industrial exposures. In fact, physicians are in the habit of prescribing much higher concentrations of synthetic chemicals than are found in industrial exposures of workers.

The drugs of the "sulfa" group are proving extremely valuable when properly used. It does not detract from their value to point out that they are far too widely and too carelessly prescribed in clinical conditions for which they are not really necessary. They have caused many cases of serious poisoning. but it has not been sufficiently emphasized that even single therapeutic doses can have marked and dangerous physiological effects. The following quotation from editorial correspondence in the Journal of Aviation Medicine (2) is significant.

"The use of sulfanilamide in the treatment of disease has increased our care of flyer problems. The British have found that a single dose reduces a pilot's ceiling about 5,000 feet. We have had one death just after, flying, from it, and one collapse. It is easily obtainable by anyone and in fact, civilian doctors prescribe it without a thought of danger in relation to flying."

If a pilot flies above his ceiling (12 000 to 14,000 feet) without using oxygen he may pass rapidly through all the early stages of action of toxic chemicals to a state of circulatory collapse. When under treatment with sulfanilamide and similar drugs he has progressed well toward stages 4 and 5 even before

flying, and a sudden decrease in oxygen supply may prove disastrous. In industrial medicine, the early action of toxic chemicals closely simulates oxygen deficiency and may lead to as drastic results as are experienced in aviation.

Further evidence of the action of sulfanilamide is given by Houghton and his collaborators: (3)

"The mental and physical handicap of taking the drug in this dosage (2-3 grams daily) is greater than the psychological and physiological tests would indicate. Aside from the vomiting in two of the six cases, each of the subjects had a feeling of considerable malaise and mental incompetence. Such feeling was not conducive to good work in the laboratory during the period of the drug and would undoubtedly impede the skilled activities of workers in industry or the military. In emergency, however, a considerable amount of unskilled labor should still be possible, provided the subjects are free from vomiting."

An editorial note in J. A. M. A. on Mental Confusion from the Sulfonamides (4) refers to a Report of the Committee on Disability and Rehabilitation, Medical and Surgical Section. Association of American Railroads, in which "it is recommended that a patient, after receiving treatment of this type, should be free from work for seven to fourteen days following such administration, before being permitted to resume duties in either engine or train service. The possibility of serious mental confusion must be borne in mind especially for those whose activities under circumstances of impaired judgment would be particularly hazardous to others. This would include many occupations in civil life and practically all those in military fields."

The effects of the "sulfa" drugs are rather lasting. We have record of at least one case in which a worker, having reached a state of circulatory collapse, failed to recover, with rest. in the normal period of 2 to 6 hours. He was under treatment with a "sulfa" drug merely because he showed an unexplained temperature rise. Actually, three weeks of rest were needed before a normal circulatory score was restored.

In a less serious degree the same situation applies to antileutic treatment with organic

arsenicals. Indeed, we wonder whether a luetic under active treatment is not in greater hazard, when exposed to harmful industrial chemicals, than one not so treated. This problem is important if there is exposure to substances (such as chlorinated hydrocarbons or aromatic nitro compounds), which may injure the liver.

SELF-MEDICATION

The use of patented drug mixtures as treatments for headaches, etc., is widespread. Some contain aniline derivatives which are quite active physiologically. Such self-medication can produce all early stages of chemical exposure and render a worker sensitive to materials to which he may be exposed in industry.

There is no need to point out that excessive indulgence in alcohol can be considered here as self-medication.

EXTREMES OF TEMPERATURE AND HUMIDITY

Unusual levels (high or low) of temperatures, and high humidity with high temperature, do not usually affect well-nourished normal persons. However, workers in the early stage of action of harmful chemicals react to high temperature (and to extremely low temperature) by rapid deterioration of circulation. In fact, a seasonal trend in the abnormality ratio obtained from the blood pressure scoring system is almost certain proof of a mass exposure to harmful material.

There are many possible causes of that trend, but the most important appear to be the following:

- (a) With increase in temperature the atmospheric concentration of toxic materials may be increased. When temperature and humidity reach such levels that there cannot be free evaporation of perspiration from the skin, there may be increased possibility of skin contact with and absorption through the skin of toxic substances.
- (b) The normal mechanism by which the body maintains its temperature involves a dilation of skin blood vessels in hot weather, and constriction of these vessels in cold weather. The peripheral blood vessels can hold a relatively large fraction of the total circulating blood. The diversion of blood to these skin vessels, on hot days may well cause

such change in the balance of circulation that, when it is added to the change already caused by toxic chemicals, a worker may develop an abnormal score.

(c) When the atmospheric temperature is very near the temperature of the skin, heat loss by radiation becomes difficult. This situation is aggravated when the air is still and humidity is high, and perspiration cannot evaporate. The perspiration then pours off the skin or is soaked up by clothes. It has been shown recently that significant quantities of vitamins C(5) and B₁(6) are lost in the perspiration so that, in extreme cases, prolonged work in hot, humid atmosphere can lead to clinically recognizable vitamin defi-Vitamins B, and C (as well as ciencies. others of the B group) are closely linked up with the oxidation-reduction processes in tissues. A relative vitamin deficiency caused by loss of vitamins in perspiration can, as has been described above, produce circulatory abnormality of the same type as, and superimposed on, that due to toxic chemicals. Further, there is evidence that, in absence of adequate vitamins B1 and C, there is a loss of ability to detoxify chemicals. In either case, extremely high temperatures and humidities may, by producing loss of vitamins, aggravate the condition already existing in men affected by industrial chemicals.

UNNECESSARY FATIGUE

Over-exercise, when away from work (especially during extremes of temperature) may have a great influence on the trend of resistance to chemicals. Often, in a routine program of study by blood pressure scoring, men are found to be in very poor condition on Monday morning, but improve greatly during the week. In spite of a minimal exposure to harmful chemicals, the work period may act more as a "rest" period than the supposed week-end rest away from work.

A very important factor in the Monday morning picture may be excessive automobile driving over the week-end. The fatigue of driving added to an improper food intake leads to physiological abnormality. There is too often, in addition, an exposure to carbon monoxide from exhaust gases. Few people pay much attention to the condition of mufflers

and exhausts in their cars and in cold weather they are apt to reduce ventilation to a minimum. It is well known that in congested traffic, significant concentrations of carbon monoxide collect in cars which follow closely in line. We have one record of a man who, after a week-end of driving, appeared at work in poor condition and suffered circulatory collapse an hour or so later, after a degree of chemical exposure which, as clearly shown by records made every two weeks for several months, would not usually give him an abnormal blood pressure score and which did not affect other men in his group on the day in question.

DISEASE

Disease due to bacterial infections or parasitic infestation is really the result of chemical poisoning and can produce all the stages of abnormality listed above. An attack of "grippe" or acute upper respiratory infection can advance a worker so far on the route of physiological change that he may react to a low concentration of a toxic chemical by a drastic fall in blood pressure score.

DEPRIVATION OF OXYGEN

Sudden reduction in the available supply of oxygen, such as occurs in flying to high altitudes, or working in restricted, unventilated enclosures, will have the same physiological effect as toxic chemicals. Added to chemical exposure, deprivation of oxygen may have drastic results. Thus, Heim (7) has shown that "concentrations of carbon monoxide which are innocuous at sea level become dangerous at even moderate altitudes." situation is not specific for carbon monoxide. It applies also to the action of hydrocarbon solvents used in the manufacture of paints and is operative when those paints are used in poorly ventilated rooms or cabins. It applies also to the household use of cleaning solvents, without proper ventilation.

THE USE OF RESULTS OF PERIODIC EXAMINATIONS

The periodic survey of blood pressure scores made as described above will indicate

- (a) occupation groups showing too many abnormal scores;
- (b) individuals showing too many abnormal scores; and

(e) individuals showing at least one abnormal score.

A preventive medical program takes care of each situation as it arises.

If the group ratio shows too many chronic men or an overall occurrence of too many abnormal scores in the nonchronic group, the immediate inference is that the group is suffering from industrial exposure to chemicals. (Only on rare occasions will it be suffering from an epidemic of disease or self-medication or alcoholism.) Immediate attention should be paid to the conditions under which the men work. These include atmospheric concentrations of toxic materials, possibilities of skin contact, efficiency of ventilating and other protective equipment such as respirators and gas masks; cleanliness of the work place and personal cleanliness of the workers, and their clothing. Steps should be taken at once to remedy any defects found. The degree to which remedies are effective will quickly be shown by blood pressure scores.

Every worker showing too many chronic examinations should be studied carefully. His place of work, his manner of working, any differences between his possible degree of exposure and that of other group members must be noted. With assistance of the personnel division, every possible inquiry should be made concerning those "external factors" described above, which may contribute to his sensitivity to chemicals. In this inquiry the worker will usually give keen and grateful cooperation, once he knows its purpose—to keep him in the best possible state of health.

If the periodic examination program is properly conducted each man should be studied whenever he gives an abnormal blood pressure score. He should be re-examined within seven days and if the second examination is abnormal, as exhaustive an inquiry should be made as in the case of a "chronically" affected worker.

While in this description greatest emphasis has been placed on the occurrence of blood pressure scores of 0.1 or less, it must not be forgotten that any downward trend of score is an index of reduced normality. The occurrence of a score below 0.20 gives a very good warning of the trend of events. Additional warnings are given by any blood pres-

sure readings on either arm which fall beyond the arbitrary limits given above.

The success of this or any other system of preventive medicine depends on unceasing vigilance and quick action when an unusual condition is disclosed.

EFFECTS OF CONTINUED ABNORMAL BLOOD PRESSURE SCORES

The physiological condition disclosed by an abnormal blood pressure score is at first merely functional. Given proper attention to its cause, it is easily reversible. Lack of attention, however, may lead to serious injury to health.

The rather anomalous situation exists that continuation of an abnormal score due to high diastolic blood pressure is often of more ultimate seriousness than continuation of abnormal scores due to low diastolic pressure. If allowed to continue, a diastolic pressure above 90 mm. may slowly rise to levels of 100 to 110 mm. even after complete removal of the worker from exposure to chemicals. Then, systolic pressure rises and there is established eventually both systolic and diastolic hypertension. Our records suggest that such conditions may be produced in workers below the age of 40 by prolonged exposure to low concentration of chemicals, which are usually considered harmless because they do not produce acute poisonings.

Continued abnormal scores due to low diastolic pressure often lead to circulatory collapse. After a time all three pressure components-systolic, diastolic and pulse pressure-fall to abnormal low levels. Inability of the circulation to compensate for changes in posture may lead to syncope by allowing the blood to pool in the lower part of the body. If a worker lies down with his head lower than his legs immediately he feels dizzy, the dizziness will disappear in a few minutes and one or two hours rest, with inhalation of oxygen or an oxygen and CO, mixture, will restore his circulation to normal. If he persists in working, his condition may become so serious as to produce a severe circulatory collapse, sometimes with fatal results.

INDEX OF CIRCULATORY BALANCE A useful index of circulatory balance is obtained by employing the ratio

Pulse Pressure

Diastolic pressure + 1/3 pulse pressure

as an index of the filling volume of the heart. Fig. 4 makes easy the reading of this index (called Volume Filling Index, V) directly from systolic and diastolic pressure. In calculating it, use the arithmetic average of the systolic pressure and the diastolic pressure at the 4th phase (change of sound) on the two arms.

Our experience shows that a value for V of 0.3 or lower indicates impending circulatory collapse. A worker may reach a value of 0.3 or less and yet, by a reflex increase of heart rate, force enough blood from the heart to prevent circulatory collapse. We consider a value of 23.0 for the product of V by the pulse rate as a useful lower limit of normal. Fig. 4 includes a table of the minimum pulse

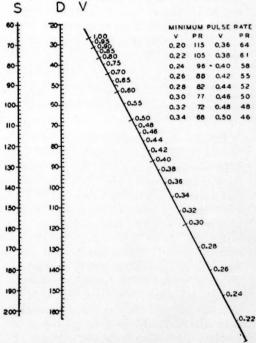


FIG. 4—Chart for calculation of filling volume index from systolic and diastolic blood pressures. To use this chart, simply stretch a piece of string or lay a transparent ruler across the chart in such a way that it cuts the reading of systolic and diastolic blood pressures and extends over to the volume index line. Read off the volume index and look at the table of minimal pulse rates to see whether or not the man's actual pulse rate is below or above that necessary for proper compensation

rates giving values of 23.0 with different values of V.

The volume filling index and its product by pulse rate are very useful in following the development of and recovery from circulatory collapse. As illustrations, consider the following:

A worker, age 43, presented himself at a plant hospital early in the morning, pallid, with unsteady gait and slightly dyspneic. He appeared exhausted and claimed he was overcome by heat. His blood pressure (measured on only one arm) was 113/75, and his pulse rate was 58. This gave him a volume filling index of 0.43. This requires a minimum pulse rate of 54 for compensation. With a rate of 58 he was obviously near collapse.

Again, a worker came to a plant hospital covered with beads of perspiration and appearing on the verge of collapse. His pulse rate was 54. His blood pressure (on one arm) was 94/70. This gave a value of 0.31 for V, requiring a minimum pulse rate of 75.

It is not implied that with values of V below 0.30, or of the product with pulse rate below 23.0, workers will necessarily collapse. But such values certainly give a limit for reference, and a warning for proper handling of individual cases.

REMOVAL OF WORKERS FROM EXFOSURE TO CHEMICALS

To remove a worker from his job because he continually shows abnormal blood pressure scores is merely to follow the path of least resistance. At the present time, such a practice can cause serious interference with production. If the scheme described above is followed properly, a man who gives an abnormal score on examination will be re-examined within a week. If the second examination again gives a bad score, investigation of the situation will be made at once and steps taken to remedy it. If, however, no solution of the problem is found by inspection of the conditions under and the manner in which the man works or by collecting all information possible on the action of "external" factors, it is advisable to remove the worker temporarily from all exposure to chemicals. The new job to which he is transferred must be physically less arduous than that from which he is re-

moved; otherwise, the increased exertion superimposed on an already abnormal circulation will prevent recovery and may even cause injury. During the period of temporary removal-which in most cases will not need to be longer than three weeks to a month -the man should be re-examined frequently; i. e., at least once a week. He should not be returned to work with chemicals until two examinations a week apart give normal scores. When this goal is reached and he returns to his previous job, he should again be examined once a week for two or three weeks. This is necessary because experience shows that a return to exposure to chemicals before adequate recovery from past action of those chemicals may lead to a sudden reduction in circulatory efficiency.

With proper conduct of the program outlined above, there should be only three causes for permanent removal from the job:

- (a) A failure to recover normal circulation within reasonable time during temporary removal from exposure.
- (b) A rapid return of abnormal scores when the worker goes back to the job atter temporary removal.
- (c) An intermittent injury or disease which renders him permanently unfit for the job.

THE SIGNIFICANCE OF ATMOSPHERIC CONCENTRATED OF TOXIC VAPORS, DUSTS, AND GASES

It will be obvious from our discussion of factors entering into the development of chronic poisoning of workers that there can be no general rule as to the atmospheric concentration of toxic vapors, dusts and gases, which can be considered safe. Yet various committees throughout the country are spending considerable time in trying to set up such so-called "safe" upper limits. These must necessarily be rather empirical figures obtained from studies of exposures to single chemicals. In industry, in the majority of cases, there are simultaneous exposures to a number of chemicals. The so-called "safe standard" can never take into account the cumulative action of the mixture of chemicals. Such "safe standards," therefore, while of use in assessing the relative efficiency of ventilation schemes, cannot be relied upon as an index of the degree to which workers are affected by their industrial exposure.

In using the blood pressure scoring system to detect minimal physiological action of chemicals, it is frequently found that there is a significant number of abnormal blood pressure scores in groups working in occupations apparently protected by very efficient ventilation systems. There may be at least two reasons for this: First, the chemical or chemicals employed may be through the skin in which case, of course, ventilation is no protection; and second, the system of ventilation used may not be such as to remove vapors or gases at their point of origin before they can be inhaled by the workers. Most frequently the ventilation system depends upon dilution by throwing into the work area large volumes of "fresh" air from outside. When we consider the information given by our blood pressure studies, we realize that the actual dilution of the vapors, while bringing them much below the so-called "safe" upper limit, may still not be adequite to prevent all action of the toxic substance upon workers. If, in addition the intake air should be contaminated by chemicals from other work areas, there is actually produced a multiple exposure which, as we have already indicated, can have pronounced effects upon the worker.

It must be emphasized that the actual condition of workers cannot be demonstrated by air analyses or by citing facts as to the efficiency of ventilating systems. It can only be discovered by periodic medical examinations, adequate to detect changes in physiology before actual injury has occurred.

* * * *

Although this system of preventive medical control of industrial exposure to toxic chemicals has required rather a voluminous explanation, in practice it is actually very simple. It has been used, and is being used, in plants employing from 100 to 2,500 men. New sources of hazard to health are being disclosed by the preliminary survey method and the efficiency of physical protective equipment is being tested and the effect of changes in production methods estimated by continuous use

of the periodic examinations with blood pressure scoring.

For the moment, this scheme has been applied only in industrial medicine. It would probably be useful also in ordinary clinical practice, especially for study of the effects of therapy, surgical treatment, or stages in the development of and convalescence from an infectious disease. It will undoubtedly be of value in aviation medicine for there the problems confronting the physician differ little from those of industrial practice.

The value of the scheme is quickly determined by proper trial. Its routine and careful use can add much information to our knowledge of the causes and development of industrial disability.

Our attempt to follow development of chronic poisoning by a study of the early physiological action of industrial chemicals has led us to the admission that exposure to chemicals may play no greater part than a number of other factors which lie outside of the worker's occupation. This should not be surprising. Man's life cannot be divided into clearcut time elements—day and night, work and play, 1935 and 1942. It is continuous. Man's physiological condition at any given instant is the integration of all that has gone before, and man's reaction, the next instant, to a change in environment necessarily depends upon the picture formed by that integration. The industrial physician trying to prevent ill health cannot confine his attention solely to the events of the work day. The sixteen hours away from the job are equally important. The worker must be told how important they are. The family physician, treating his patient for a non-occupational condition, should remember that his therapy may also influence the patient's industrial life.

Maintenance of health in industry is a collective responsibility. Worker and employer, plant physician and family doctor all have a part to play, and each one's manner of playing may affect the others. Now that our very existence as a free nation depends on the output of war industries, and that in turn upon continuity and efficiency at the job, we must each accept our part in our collective responsibility. There has never been a greater op-

portunity for the highest type of medical service.

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ACUTE AGRANULOCYTOSIS DUE TO SULFADIAZINE

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Sulfadiazine has been widely used because of its greater clinical application in a variety of infections and also because of the earlier reports of freedom from some of the more common toxic reactions such as nausea and vomiting. Only two cases of agranulocytosis due to its use have so far appeared in the literature (1)-(2).

It may be of interest to record another case of sulfadiazine-agranulocytosis. This curred in a patient when the blood concentration of the drug was at a relatively low level (6.5 mgm. of free sulfadiazine per 100 cc of blood.) It is also of interest because of the prompt return of the white counts to normal after therapy.

REPORT OF CASE

A 37-year-old, white male American was admitted to St. Francis Hospital, Wilmington, on the medical service on June 10, 1942, with the chief complaint of extreme fatigue of many months duration. Except for scarlet fever during childhood and a tonsillectomy in July, 1941, the patient had been perfeetly well until the fall of 1941 when he first complained of gradually increasing fatigue for which he was admitted to the Wilmington General Hospital in January and discharged in March, 1942. Following this he felt much improved until the end of April, 1942. At this time he had pains in the knees and ankles, associated with edema and mild red discolora-

tion around the metatarsal joints. He was treated at home without absolute bed rest and temperatures were not recorded. There was no history of venereal or rheumatic disease but during his first hospitalization in January, several blood cultures were positive for streptococcus viridans. The family history was essentially irrelevant.

Examination showed an undernourished white male appearing moderately sick, mentally alert and cooperative. The temperature was 100° F; pulse rate, 122; respiration, 24; and blood pressure 104/58. His skin had a yellow-grayish color, and was rather dry and rough. No petechiae could be found. The pupils were round, equal, and reacted promptly to light and accommodation. The conjunctivae were pale and not injected. The tongue was clear, the tonsils had been removed, and no lymphnodes or enlargement of the thyroid gland were noticeable. The lungs were clear throughout on percussion and auscultation. The heart was in the normal limits of size, with a prominent systolic thrill at the apex and in the aortic area. A loud rough systolic murmur covered the first sound in the apical region and both sounds in the aortic area. At the pulmonary ostium the first sound was split and a loud systolic murmur was audible.

The abdomen was soft, relaxed, and the liver was not enlarged. Although there was some tenderness in the left upper quadrant, the spleen was not palpable but was percussible over a surface of about 6-8 cm. Some ankle edema was present without any regional discoloration or increase in temperature.

The blood Wassermann and Kahn reactions were negative. The urine was alkaline, with a faint trace of albumen, and was negative for sugar, with only a few white blood cells present per high-power field.

The sedimentation rate was 44 mm. in 30 minutes.

The red cell count was 3,100,000. White cell count 7,650 with 78% polymorphonuclears, 19% small lymphocytes, 2% large lymphocytes, 1% monocytes and 60% hemoglobin. A blood culture taken on the day of admission revealed the presence of nineteen colonies of streptococcus viridans in 2 cc. of blood after two days incubation. The patient

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was typed and an adequate list of compatible donors secured as the treatment was outlined.

Two days after admission sulfathiazole was started. Two grams of the drug were given by mouth every four hours, but had to be discontinued thirty-six hours later because of vomiting. Sodium sulfathiazole was then given intravenously, gram 1 every eight hours, and the dose was increased to grams six daily in three injections. After two days blood sulfathiazole concentration reached a level of 6.4 mgm. and there was a reduction in the temperature curve. On June 23rd the patient refused further intravenous therapy, and sulfadiazine, more easily tolerated, was started orally beginning with 4 gms, for the first dose and one gram at three or four hour intervals according to the blood level which had been checked every other day (see table). On June 23rd administration of typhoidparatyphoid vaccine was started with 0.2 cc and gradually increased to 0.4 cc, 0.5 cc, 0.6 ce, 0.8 ce, 1 ce, and 1.4 ce on July 8, without appreciable changes in the temperature curve or blood culture. Accessory therapeutic measures such as high caloric, high vitamin diet, daily injections of liver extract, stimulation, and blood transfusions had been given during the course of the treatment.

Because of a change in personnel, a sore throat, that had been present for two days, was not reported until July 16. Examination at this time revealed only a slight reddening of the pharynx and beginning ulceration around the gum margin of the left lower molars. The white cell count was 2,350. Sulfadiazine therapy was immediately discontinued and adequate doses of pentnucleotide given intramuscularly. The next day immediately following the administration of 10 cc of pentnucleotide, the patient developed a marked reaction characterized by fainting which gradually merged into unconsciousness. As it was feared that pentnucleotide medication might have to be discontinued because of this sensitivity, it was thought advisable to try the induction of a sterile abscess. The purpose was to mobilize the white cells after stimulation of the hematopoietic system had been started. The same day 4 cc of autoclaved turpentine were injected into the left rectus muscle between the

umbilicus and the anterior-superior spine of the ileum. Reference to the table will show that from July 17, 1942 to July 22, 1942, inclusive, there was a gradual diminution in the total white count with an absence of nucleated white cells in the blood smears for two consecutive days. Daily transfusions were given and pentnucleotide continued with caution.

On July 24 the patient began to complain of pain in the area of injection. At this time a sharp rise in the total white blood count and also in the percentage of polymorphonuclears was noticed. The patient's general condition was much improved, the temperature dropped to normal, but therapy was continued for a few days in spite of the high blood counts. A week later, when marked infiltration of the left flank was present, an aspiration of 1 cc of fluid was made. The bacteriological examination revealed no organisms. No attempt to evacuate this "pus" was made because it was felt advisable to leave a reserve of white cells. A blood culture taken on August 5 was positive for viridans. streptococcus Neoarsphenamine was administered with increasing doses given intravenously three days apart, accompanied by a subjective improvement in general status.

On August 18 the left flank was aspirated and about 75 cc of brownish sterile pus was obtained, followed by a slight drop in the leukocyte count without appreciable changes in the percentage of polymorphonuclears.

A week later under local superficial infiltration a small incision was made through the center of the fluctuating area. The edges of the wound were spread with a Kelly forceps and more than 500 cc of sterile pus was evacuated. A rubber drain was inserted. Two successive examinations showed a decrease in the leucocyte count.

On September 3rd the patient's condition suddenly became worse. He began to complain of blurring of the vision and nausea. The pulse became weak and the respirations shallow. Stimulants were administered. On September 5th he had three convulsive seizures. He died suddenly the next day of cerebral embolism. No permission for a postmortem examination could be obtained.

DISCUSSION

The importance of a close check on all patients receiving intensive therapy with the sulonamides is emphasized by the development of acute agranulocytosis in this patient in spite of daily alternate blood counts and sulfadiazine levels of the blood, daily injections of liver extract, and frequent transfusions, measures often used in the therapy of agranulocytosis.

The value of the production of a sterile abscess to mobilize leucocytes after maturation had been stimulated by adequate doses of pentnucleotide in the treatment of agranulocytosis has been questioned by Beckman (3). It may be of significance, however, that there occurred a sharp drop in the total white count when the abscess was evacuated. (chart).

Date 1942	RBC in millions	WBC	Poly's	SI%	LL%	Mono %	Myel %	Hgb	Sulfa. Level	Temp. Daily	Blood Trans. in cc	TREATMENTS
1942	millions										m ee	
6-11	3'11	7650	78	19	2	1		60		100.3		
6-15	0.11	.000		10	_	-		00	0.7	100		Sulfathiazole Blood Culture
6-16		9750						64		100.2		positive for Strep. Viridans.
6-17									5	99.3		
6-18		10650						60		100	500	
6-19									2.7	100		
6-20		10100						61		99.4		Sulfathiazole Stopped
6-22		10400						CA	6.4	100	200	Sulfadiazine & Soda Bicarb.
6-23 6-24		10400						64	5.2	100.2 100.2	300	Typh. & Para. Vaccine 0.2 cc
6-25		11000						64	0.2	102		Typh. & Para. Vaccine 0.4 cc
6-26		11000						01	4.1	99		Typii. & Tara. Vaccine 0.4 cc
6-27		10800						64		100.2		Typh. & Para. Vaccine 0.5 cc
6-29	3'30	9800	82	13	2	3		64	5.4	100.2		Typh. & Para. Vaccine 0.6 cc
6-30										99	200	
7-1										100.2		Typh. & Para. Vaccine 0.8 cc
7-2									õ	100		
7-3		6850						68	- 1	99.3		Typh. & Para. Vaccine 1 cc
7-4		7000						OA.	5.1	$100.2 \\ 99.1$		
7-6 7-8		7900						64		99.4		Typh. & Para. Vaccine 1.4 cc
7-9		8400						61		99.4		Typii. & Tara. Vaccine 1.4 cc
7-10		0100						01	5.3	99.3	250	
7-11		6200						68		100		
7-13									6	101.1		Blood Culture positive after
7-14		3500						67		101.3		four days incubation
7-15									6.5	101.4		~
7-16		2350						58		102	0.50	Sulfadiazine discontinued
7-17		2400	6	82	8	4				102.1	250	Pentnucleotide 40 cc
7-18 7-19		$\frac{2600}{2250}$	0	89 88	5	6				102.3	500 150	Turpentine 4 cc-Pentnucl. 10 cc Pentnucleotide 20 cc
7-19		1450	0	88	7	5				103.1	150	Pentnucleotide 20 cc
7-21		1400	0	00		J				101.2	100	Pentnucleotide 20 cc
7-22	3'67	2850	22	64	7	6	1	75		102.4	200	Pentnucleotide 20 cc
7-23										101		Pentnucleotide 20 cc
7-24		8200	80	15	3		2			99	250	Pentnucleotide 10 cc daily
7-27		10250	82	16	2					99		Pentnucleotide 10 cc
7-29		15500	83	14	3					100		
8-8										99 100		Neoarsphenamine 0.15 gms.
8-11 8-13		7750	81	15	4					100.1		Neoarsphenamine 0.30 gms.
8-14		1100	01	10	4					100.1		Noonanhanamina 0.45
8-17		11600	84	11	3	2				101		Neoarsphenamine 0.45 gms.
8-18		11000	0.			-				100		75 cc pus removed Neo. 0.45
8-21		7200	79	17	4					99		to ce pas removed neo. 0.45
8-22										99.2		Neoarsphenamine 0.45 gms.
8-25		10000	87	9	2		2			99		550 cc pus evacuated
8-27										99.1		Neoarsphenamine 0.45 gms.
8-29		5500	84	16						99.3		
8-31 9-1		3850	74	22	2	2				98.4		Neoarsphenamine 0.45 gms.
9-1		3030	14	44	4	4				98.3		

SUMMARY

The third case of acute agranulocytosis following sulfadiazine therapy is presented. This occurred in spite of adequate measures for its prevention. Pentnucleotide therapy, with induction of a sterile abscess, proved effectual in restoring the blood count to normal and improved the general status of our patient. Death was due to a cerebral embolism.

REFERENCES

- M. Levin & F. H. Bethell: Fatal Granulocytopenia Developing During Administration of Sulfadiazine (Sulfanilamide Derivative), Univ. Hosp. Bull., Ann Arbor, 8: April, 1942.
- John J. Curry: Acute Agranulocytosis following Sulfadiazine, J. A. M. A., 119: 1502, August, 1942.
- Beckman: Treatment in General Practice, 4th edition, W. B. Saunders Co., 1942, p. 627.

ARMY'S 1943 PROGRAM

The 1943 recruiting program of the Surgeon General of the Army calls for the commissioning of 6,900 physicians and approximately 3,000 hospital internes and residents, it is reported in *The Journal of the American Medical Association* for March 13 in an outline of the new procedure of processing physicians, dentists and veterinarians for the Army. The program also calls for the commissioning of 4,800 dentists and 900 veterinarians.

Physicians will be procured from the following twenty states and the District of Columbia: California, Colorado, Connecticut, Illinois, Iowa, Maryland, Massachusetts, Minnesota, Missouri, Nebraska, Nevada, New Hampshire, New Jersey, New York, Ohio, Oregon, Pennsylvania, Rhode Island, Vermont and Wisconsin.

The following states have already contributed more physicians to the armed forces than the sum of their 1942 and 1943 quotas and will not be called on to furnish any more physicians, except internes and residents and except special cases for specific position vacancies, during 1943: Alabama, Arizona, Delaware, Georgia, Idaho, Kentucky, Louisiana, Mississippi, New Mexico, North Carolina, South Carolina, Tennessee, Texas, West Virginia and Wyoming.

It is stated that at present there will be no procurement of physicians, except internes and residents and in special cases for specific position vacancies, in those states not listed above. There will be no procurement of dentists, except special cases for specific position vacancies, in the following sixteen states: Alabama, Arizona, Arkansas, Delaware, Florida, Georgia, Kentucky, Louisiana, Mississippi, New Mexico, North Carolina, Oklahoma, South Carolina, Tennessee, Texas and Virginia.

At the present time there are no restrictions on the recruiting of veterinarians.

In the instructions issued by the Army it is pointed out that the Surgeon General has discontinued all medical officer recruiting boards and that under the new procurement program no physician, dentist or veterinarian will be commissioned in the armed forces of the United States until he has been declared "available" by the Procurement and Assignment Service of the War Manpower Commission.

In each state the Procurement and Assignment Service has set up three state chairmen: medical, dental and veterinary. Each of these prepares a monthly quota list of physicians, dentists and veterinarians who are apparently suitable and who are available, for commissioning in the Army of the United States. This list is submitted to the central office of the Procurement and Assignment Service which sends a communication inviting such individuals to apply for service with the armed forces. On the reply card enclosed with the invitation the individual states his preference for the Army, Navy or Medical Department of the Air Forces. These reply cards are sent by the potential applicants to the state chairmen of the Procurement and Assignment Service who in turn submit lists of such potential applicants to the Officer Procurement Service of the Army.

On receipt of such lists the officer procurement district office contacts the potential applicant and arranges for an interview regarding a commission.

Applicants will be requested by the officer procurement district office to complete all papers and take all steps required of them within fourteen days of the date of such request. If this is not complied with, a report thereon will be transmitted by the officer procurement district office to the state chair-

men of the Procurement and Assignment Service.

The decision as to the grade and appointment to be recommended for each candidate rests with the Surgeon General, not with the Officer Procurement Service.

THE SUPREME COURT DECISION

By this time all should have read in the Journal of the American Medical Association, January 23, 1943, issue, page 267, the text of the opinion (U. S. Supreme Court) affirming guilt of two medical societies.

Since the final decision of the Supreme Court of the United States has been given in disposition of the suit against the District of Columbia Medical Society and the AMA charged with conspiracy to restrain in trade the activities of a Washington, D. C., Group Health Association formed to supply prepaid medical and hospital service to its membership, it is unnecessary to comment specifically on the Court's decision.

Many members of the AMA seem to be pleased that the unanimous opinion of the Court was written by a Pennsylvanian, a learned judge, not to be influenced by attitudes toward many New Deal policies which most physicians may have believed inspired the original prosecution.

Physicians will accept the dictum that they were in error as practitioners of medicine to dissociate themselves, by official action in their societies, from professional relationships with other physicians employed by insured groups to render professional service to subscribers.

It is said that the operation of Group Health Association attracts no attention from the practicing physicians in the District of Columbia. It is known that they advertised recently in the *Journal of the AMA* for physicians to accept appointments in their service, and that the total number of subscribers after its four or five years in business totals 3300, which seems an indifferent response from a city said to house more than 750,000 of government employees.

The experience of the combined non-profit limited medical service and hospital service in the State of Michigan under the control of the profession of that state has fared much better, having at the present time in the third year of its existence 600,000 subscribers and more than 3000 participating physicians.

The physicians of California, Massachusetts, Michigan, New Jersey, New York and Pennsylvania, with their own plans now selling non-profit insured medical and hospital service to groups, will, no doubt, since receiving the opinion of the Supreme Court, develop an even more lively interest in the success of their own service plans.

In the meantime we should feel privileged to enjoy the widely publicized comments of others on some of the implications of the Court's decision.

An editorial appearing recently in the Wall Street Journal comments under the caption "With Clubs It's Legal." The editorial refers to a recent ruling of the Supreme Court of the United States to the effect that so far as Federal statutes go the requirement that a farmer or other producer hauling his produce into New York City shall be stopped to take on and pay a member of the local teamsters' union, is perfectly legal, and that the Federal Government could not interfere. Truck owners who have resisted paying this tribute have suffered damage to their vehicles and destruction of their cargoes, while the consumers in New York pay this union tribute in higher prices.

The editorial continues: "The organized physicians in the District of Columbia were charged with attempting to prevent the members of their association from accepting employment under the Group Health plan and to restrain hospitals from affording facilities to patients of physicians employed under the plan. The Supreme Court ruled that the organized physicians violated the Sherman Anti-trust Act."

Continuing, the editorial states: "We do not raise the question as to whether the Court correctly interpreted the law in each case, but apparently the Washington physicians should have organized a union; the union officials then hire a group of pluguglies; these goons could then have beaten up the physicians who did not conform to union rules and they could have picketed the hospitals and refused to let supplies be taken to

(Concluded on Page 48)

Editorial

DELAWARE STATE MEDICAL JOURNAL

arawings for illustrations must be carefully marked and show clearly what is intended.

Footnotes and bibliographies should conform to the style of the Quarterly Cumulative Index Medicus, published by the American Medical Association, Chicago.

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Vol. 15

MARCH, 1943

No. 3

FALSE POSITIVES

The matter of false positive serological reactions in the test for syphilis is usually dismissed in this latitude with the remark that malaria, yaws and leprosy are rare in Delaware. In the most competent hands modern serological tests provide from 0.2 to 1 per cent technical false positive results in known non-syphilitic persons. It is pre-supposed that any single positive reaction which is unsupported by history or clinical evidence will be checked in the same laboratory or another laboratory utilizing two or more different tests. A transient false positive reaction in infectious mononucleosis is of practical interest because of the not uncommon occurrence of that disease at present. Lynch, Boynton and Kimball⁽¹⁾ report 16 per cent false positive reactions in a variety of tests and with well controlled procedures among 263 persons following smallpox vaccinations. These reactions reached their peak from the

22nd to the 28th day following vaccination in the case of the Kolmer Wassermann and Kahn tests and in a few the reactions were still positive after four months. They are, therefore, not to be detected merely by repeating the test. With the recent local widespread vaccination of adults it is therefore natural that false positive Wassermann and Kahn reactions from this source have come to light in Wilmington and Baltimore. In Philadelphia, Favorite⁽²⁾, studying 202 individuals following vaccination found originally 9.4 per cent of false positives, and by reexamining later 30 of these individuals the false positives rose to 11.3 per cent, during a period of 57 days. Even the provocative test has been toppled from its pedestal with the confirmative work of Barnett and Kulcher (3) showing syphilitic reagin in normal blood and a false positive provocative effect following intravenous injection of neoarsphenamine. Not yet in the literature are oral communications from staff members of two teaching institutions that, "patients convalescent from virus-pneumonia are showing a higher percentage of positive luetic serological reactions than the general population."

That these false positive reactions are of practical frequency is shown by the fact that Kahn is advocating a "Verification Test" which is designed to pick out the blood giving a postive serologic reaction unrelated to syphilis. Other serologists are attempting to develop the same type of confirmatory tests.

With the serological tests for syphilis in this status it is not surprising that states which have passed laws compelling premarital examination for syphilis have found that a considerable number of non-syphilitic persons are caused undue alarm, delay in marriage, and expense in unraveling the significance of false positive or doubtful results.

1. Lynch, Francis W. et al.: False Positive Serologic Reactions for Syphilis Due to Smallpox Vaccinations (Vaccinia), J. A. M. A., 117: 951, (Aug. 23) 1941.

2. Favorite, Grant O.: Effects of Smallpox Vaccination on the Serologic Tests for Syphilis, Phila, Med. 30: 853. March 13, 1943.

3. Barnett, C. W. et al.: Quantitative Provocative Reactions in Normal and Syphilitic Sera Following the Injection of Neoarsphenamine, Am. J. Syph., Gonor. & Ven. Dis., 22: 712, (Nov.) 1938.

O. C. D. NOTICE

TO THE MEDICAL FRATERNITY OF DELAWARE:

New legislation has been enacted extending benefits, relief and medical care to workers involved in the United States Civilian Defense Corps, who are injured in test blackouts and air raids, as well as injury or death occurring from enemy action. In order to secure these benefits it is necessary that each person take the prescribed oath of office, which will be mailed to him, so he can be enrolled by the Personnel Office.

It is therefore requested that each physician sign the oath, reproduced below, and return it promptly to the Chief of Emergency Medical Service, State Council of Defense, 839 King Street, Wilmington, Delaware.

Oath of Office Medical Division

State Council of Defense (O. C. D.)

I do solemnly swear (or affirm) that I will bear true faith and allegiance to the United States of America, that I will serve them honestly and faithfully against all their enemies whomsoever, and that I will obey the orders of the President of the United States and the orders of the offices appointed over me

Sign

(Approve CHIEF SERVI	,]	0																
Please	answei	r	t	h	e	f	0	11	0	V	/i	n	g							
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Name of	Wife																			
No. of C																				

Your prompt cooperation will be appreciated.

MEREDITH I. SAMUEL, M. D., Chief, EMS.

OBITUARY

Augustus H. Bishop, M. D.

Dr. Bishop, the oldest practitioner of medicine in Delaware, died in the Kent General Hospital, Dover, on March 13, 1943, in his 91st year, following a heart attack a week earlier. Despite his advanced years, he had been active in his practice until this attack.

Born near Fenwick, the son of the late Captain and Mrs. James Bishop, Dr. Bishop was graduated from the University of Pennsylvania Medical School in 1875. He began the practice of medicine and surgery with the late Dr. William P. Parvis at Leipsic, but soon located in Dover.

Dr. Bishop was a member of the Kent County Medical Society, the Medical Society of Delaware and of the American Medical Association.

He is survived by two daughters, Mrs. Helen B. Hughes, Dover; and Miss Elsie Bishop, New York; three grandchildren, Mrs. Dyre Bradford, Wilmington; Miss Louise Hughes, Dover, and William A. Hughes, Rehoboth Beach, and a great-grandson, William A. Hughes, Dover. Dr. James R. Bishop, Salisbury, is a nephew.

Funeral services were held on March 15, 1943, at his home in Dover, with interment in Christ Church yard. The officiating clergyman was the Rev. B. F. Thompson, assisted by the Rev. Paul A. Kellogg.

THE SUPREME COURT DECISION

(Concluded from Page 46)

them. In all of these activities they would have been immune from Federal prosecution. What reason is there to believe that Washington, where unions have such powerful friends, would be an exception?"

"Well," concludes the editorial, "at any rate the good doctors of Washington now know who constitute the 'underprivileged."

—Phila. Med., Feb. 27, 1943.

BOOK REVIEWS

The Anatomy of the Nervous System. By Stephen W. Ranson, M. D., Ph. D., formerly Professor of Neurology and Director of Neurological Institute, Northwestern University Medical School. Seventh edition, Pp. 520, with 408 illustrations. Cloth. Price, 86.50. Philadelphia: W. B. Saunders Company, 1943.

This text continues its work for the medical student as a soloist in this field. Rare is the student who prides himself on his knowledge of brain anatomy, but when he is asked a question on the subject his mind automatically goes back to Ranson's where an illustration in this well-known text may or may not

come to his imaging faculties to prevent his lowly reputation as a knower of intellee tual anatomy from sinking to a new low. In this edition the material has been thoroughly revised and brought up to date. The cuts and illustrations are excellent. The writer has made every effort to simplify the description of this subject. Science today is more than ever correlating brain anatomy with psychology, neurology, and psychiatry, and more and more the grey-haired clinician finds himself going back to basic texts in brain anatomy and physiology. Ranson's book is invaluable for this purpose.

Textbook of Clinical Neurology. By Israel S. Wechsler, M. D., Clinical Professor of Neurology, Columbia University. Fifth edition. Pp. 840. Cloth. Price, \$7.50. Philadelphia: W. B. Saunders Company, 1942.

This practical manual is a valuable and handy work for quick reference or more detailed study. It is systematic, well arranged, accurate and brief. The text has been thoroughly revised to include the essential findings and recent work in this field. The chapters dealing with interpretation of signs and symptoms, psychometric tests, and history of neurology add much to make this work interesting and instructive. The chapter on injuries of the brain does its part to convince the reader that a person may suffer severe injury to the brain without brains, bone, and blood being scattered all about the scene of the accident. An excellent book for the busy medical student and physician.

Orthopedic Subjects: Military Surgical Manuals, Volume IV. Edited by George E. Bennett, M. D., Chairman. Pp. 305, with 79 illustrations. Cloth. Price, \$3.00. Philadelphia: W. B. Saunders Company, 1942.

Burns, Shock, Wound Healing, and Vascular Injuries: Military Surgical Manuals, Volume V. Prepared under the auspices of the Committee on Surgery. Pp. 272, with 82 illustrations. Cloth. Price, \$2.50. Philadelphia: W. B. Saunders Company, 1943.

These two volumes are part of a series of six, prepared by the Committee on Surgery of the Division of Medical Sciences of the National Research Council. Being military manuals the stress is naturally on treatment, as agreed upon by the respective subcommittees,

composed of outstanding authorities in their respective fields. These texts therefore are authoritative, up to date, and non-controversial. Furthermore, they are concise, and therefore meaty. Like the others that have appeared in this series they are heartily recommended to practitioners interested in their respective fields.

Nutrition Yardstick. Prepared by the National Live Stock and Meat Board. Pp. 24. Paper. Price, \$1.00. Chicago: National Live Stock and Meat Board, 1943.

This is a graphic calculator for measuring the food value and adequacy of daily diets, and consists of an ingenious arrangement of pull slides and tables from which are obtained the total daily values of the protein, calories, minerals, and vitamins. It is easy to understand, simple to work and gives accurate results, and is approved by the Council on Foods and Nutrition of the A. M. A. Quicker than the ordinary tables alone, it will be of value to physicians, dietitians, nurses, and to those laymen charged with the duty of accurate appraisal of their diets.

The Reichert Collection—Handbook. 72 Pp., with 8 illustrations. Paper. Price gratis New York: Burroughs Wellcome & Company, 1943.

This is a Handbook on the Reichert Collection, illustrative of the evolution and development of diagnostic instruments and techniques in medicine. The Collection itself is now on view as a loan exhibit at the Wellcome Exhibition Galleries.

The Handbook deals with sphygmography, sphygmomanometry, auscultation, microscopy, and endoscopy, and, because of its completeness and detail in tracing the evolution of diagnostic instruments, is a valuable contribution to the subject. It is designed for use by students, libraries, museums and other agencies, and physicians who are interested in the historical aspects of the development of the instruments and techniques of physical diagnosis. The distribution of the Handbook is complimentary but will be limited to members of the medical and allied professions.

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